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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,932	11/16/2005	Minoru Moriya	BY0025P	3754

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

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06/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/556,932	MORIYA ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14-21 and 25-27* is/are allowed.

6)☒ Claim(s) *22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060207*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 14-27 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating obesity, does not reasonably provide enablement for a method of antagonizing the melanin concentrating hormone receptor in a subject; or a method of **preventing** or treating a condition from metabolic disorders, cardiovascular disorders, central nervous system or peripheral nervous system disorders, reproductive disorders, digestive disorders, respiratory disorders, cancer, and pigmentation generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the

claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The specification fails to enable one skilled in the art to use the claimed compounds. The use disclosed in the specification is that the instant compounds inhibit the binding of MCH to MCH-1R, and therefore useful as therapeutic agents, etc., see pages 3-4. Test assays to measure MCH binding inhibition activity is provided at pages 41-42, however, there in nothing with regards to how this data can be extrapolated to the **prevention** or treatment of various conditions of the instant claims - metabolic disorders, cardiovascular disorders, central nervous system or peripheral nervous system disorders, reproductive disorders, digestive disorders, respiratory disorders, cancer, and pigmentation generally. The data provided in the specification is insufficient such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the instantly claimed compounds. This area of receptor activity is highly structure specific and unpredictable as can be seen from the range of the results obtained for the tested compounds. Further, there is no evidence on record which demonstrates that the *in-vitro* screening tests relied upon are recognized in the art as being reasonably predictive of success in any of the contemplated areas of inhibiting MCH-1R. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study"). In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one

having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds as MCH antagonists.

The instant claim 22 recites "a method of antagonizing melanin concentrating hormone receptor" and claims 23-24 recite 'a method of preventing or treating a condition selected from: metabolic disorders, cardiovascular disorders, central nervous system or peripheral nervous system disorders, reproductive disorders, digestive disorders, respiratory disorders, cancer, and pigmentation'. The instant claims appear to be 'reach through' claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through to the corresponding therapeutic method of any or all diseases, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

The instant claims are drawn to a method for treatment of 'a metabolic disorders' and the specification provides a select list of disorders such as obesity, diabetes, hyperlipidemia, hyperglycemia, etc. However, the instant claim includes disorders that are known to exist and those that may be discovered in the future and therefore, is extremely broad. The claims cover "disorders" that are known to exist and those, that are yet to be discovered and therefore, the use of the term is extremely broad. Some of the 'metabolic disorders' associated with the mechanism stated in the claims include the following:

- Hyperlipidemia. High blood levels of cholesterol and triglycerides.
- Hypertriglycerdemia – high levels of triglycerides in blood.
- Non-insulin dependent diabetes mellitus (NIDDM)- a long-term metabolic disorder that is primarily characterized by insulin resistance, relative insulin deficiency, and hyperglycemia.

'Cardiovascular diseases' embrace a vast array of problems, many of which are contradictory to others. Thus, it covers hypertension and hypotension. It covers various types of arrhythmias; angina pectoris', the thrombotic symptoms of diabetes, atherosclerosis and hyperlipoproteinaemias, ischemic heart disease including congestive heart failure and myocardial infarction, stroke, and peripheral vascular disorders, such as deep-vein thrombosis and thrombophlebitis percutaneous transluminal coronary angiography (PTCAI; elevated blood levels of triglycerides, of total cholesterol or of LDL cholesterol, arteriosclerosis, peripheral vascular disease, cerebral vascular disease and pulmonary hypertension, migraine, cardiomyopathy, etc. Not one compound -- let alone a genus of trillions of compounds, could possibly be effective against such disorders generally. However, the instant claim includes disorders that are known to exist and those that may be discovered in the future and therefore, is extremely broad. For example, regarding arteriosclerosis, a state of the art online reference states "the relationship between blood cholesterol levels and arteriosclerosis is not fully understood" (see http://www.infoplease.com/ce6/sci/A0804864.html).

It is revolutionary for a compound to be effective as an agent that modulates, elevates and lowers the glucose levels. The specification did not provide any competent tests or data to establish that the compounds have the claimed 'glucose modulating activity'. A state of the art reference indicates that "Although the treatment options for Type 2 diabetes have expanded rapidly in recent years with the development of new oral therapies, the abilities of these agents to lower blood glucose to reach and sustain glycemic targets is limited", see <http://www.endotext.org/diabetes/diabetes24rosenstock/diabetesframe24rosenstock.htm>.

The instant claims are read on many therapeutic methods, for example, a method of

preventing or treating **cancer**. No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). A 'disorder characterized by abnormal cell proliferation' is anything that is caused by abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, polyps, etc. Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers or abnormal cell proliferative disorders generally.

By way of the MCH antagonizing activity, the instant compounds are claimed to be useful in preventing or treating various types of disorders. However, there is no nexus in the specification how this activity relates to all types of diseases of the claims, such as secondary causes of diabetes, cardiovascular diseases, etc. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor

activity is generally unpredictable and highly structure specific area, and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the other methods of treatment of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein and therefore, require the treatment. Next, applicant's attention is drawn to the "Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001" wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly intended therapeutic and preventive methods solely based on the insulin secretion stimulating activity disclosed for the compounds. The state of the art reference Kowalski et al. (cited in IDS) regarding the 'therapeutic potential of melanin concentrating hormone-1 receptor antagonists' provide that 'preclinical data suggests that MCH-1R antagonists will be efficacious for the treatment of obesity' (see page 1115). Regarding the use of MCH-1R antagonists for other contemplated therapeutic methods the reference indicates that "there are a number of issues that need to be addressed" (see page 1119).

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24

(CCPA 1970).

Further, the instant claims are drawn not only to 'a method of treating' but also to '**a method of preventing** metabolic disorders, cardiovascular disorders, central nervous system or peripheral nervous system disorders, reproductive disorders, digestive disorders, respiratory disorders, cancer, and pigmentation', for which the specification does not provide sufficient enablement. 'To prevent' actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the recited effect of **prevention**. Based on the inhibitory activity, the instant compounds are disclosed to be useful in the "prevention" of, for example, degenerative disorders, for which applicants provide no competent evidence. It is inconceivable from the *in vitro* data of a small number of representative compounds can be correlated to the "treating or **preventing**" of the various claimed disorders, such that the claimed compounds can not only treat but also "prevent" a myriad of diseases associated with the stated activity. Further, there is no evidence on record which demonstrates that the *in-vitro* screening test relied upon is recognized in the art as being reasonably predictive of success in any of the contemplated areas of "preventing". Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study").

Part of the difficulty of developing drugs effective for **preventing** any of the medical conditions such as metabolic disorders, cardiovascular disorders, central nervous system or

peripheral nervous system disorders, reproductive disorders, digestive disorders, respiratory disorders, cancer, and pigmentation, lies in the lack of understanding as to why people come down with these disorders and the numerous causes of these disorders.

The diagnosis of each of the disease is generally suggested by medical history and reports of endoscopy, cytology, X-ray, biopsy, etc. depending on the symptoms, signs and complications, which is essential to establish the dosage regimen for appropriate treatment or prevention. The disclosure does not provide any guidance towards the dosage regimen required to facilitate the treatment and/or inhibition of the claimed disorders, nor indicate competent technical references in the appropriate methods.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed methods.

Allowable Subject Matter

Claims 14-21 and 25-27 are allowed. The references of record do not teach or fairly suggest the instantly claimed compounds.

Receipt is acknowledged of the Information Disclosure Statement filed on February 7, 2006 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

June 25, 2008